

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Billiar et al.	Art Unit	: 1618
Serial No.	: 10/676,280	Examiner	: Blessing M. Fubara
Filed	: September 30, 2003	Conf. No.	: 7071
Title	: TREATMENT FOR HEMORRHAGIC SHOCK		

Commissioner for Patents  
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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants request review of the final rejection in the above-identified application of:

(1) claims 1-3, 10, and 11 as allegedly anticipated by either Fujita et al., Nature Medicine, 7:598-604, 2001 ("Fujita") or Pinsky et al., US 2005/0048133 ("Pinsky") as allegedly evidenced by Bar-Or et al., US 2005/0215468 ("Bar-Or"); (2) claims 1, 55, and 56 as allegedly obvious over either Fujita or Pinsky; and (3) claims 1, 2, and 57-65 as allegedly obvious over Fujita or Pinsky in view of Peitzman et al., Curr. Probl. Surg., 1995, 32: 925-1002, abstract ("Peitzman").

I. The Office Has Made Errors of Both Fact and Law in Its Rejection for Alleged Anticipation

Claims 1-3, 10, and 11 were rejected by the Office as allegedly anticipated by Fujita, and claims 1-3 and 10-14 were rejected as allegedly anticipated by Pinsky, both as allegedly evidenced by Bar-Or. Applicants respectfully submit that the Office has committed at least four substantive errors, two of fact and two of law, which led to incorrect findings of anticipation. The first factual error is that the Office has deemed "hemorrhagic shock" and "ischemia" to be one and the same condition. The second factual error is that the Office has misinterpreted Fujita and/or Pinsky, leading the Office to conclude that these references disclose experiments wherein hemorrhagic shock is treated with carbon monoxide (CO). The first error of law is that the Office has misapplied the standard for inherent anticipation. The second error of law is that the Office has refused to consider a declaration signed by Brian Zuckerbraun, M.D., which sought to explain to the Office how one of skill in the art would define hemorrhagic shock.

In its rejection over Fujita, the Office Action mailed April 16, 2009 (hereinafter, "the Office Action") states:

Fujita discloses that inhaled CO protects against ischemic lung tissue injury (see the whole document). Inhalation meets claim 3 and lung tissue injury meets claim 1. Since ischemia is not limited to one organ and can be more generalized as in e.g. hemorrhagic shock as evidenced by Bar-Or et al. (US 2005/0215468) in paragraph [0004] where it describes ischemia occurs in hemorrhagic shock in a

more generalized sense. Thus Fujita meets claims 1-3, 10 and 11 because treating ischemia that occurs in hemorrhagic shock inherently treats the condition of hemorrhagic shock.

The Office Action at page 8, *sic* throughout. Regarding the rejection over Pinsky, the Office Action states:

Pinsky treats tissues damaged (paragraph [0099], [0164]) by ischemic disorders (paragraph [0017]) with carbon monoxide inhalation (paragraphs [0028]-[0030], [0049], [0055], [0061], [0062]). Ischemia is shown by the prior art to be generalized conditions deriving from hemorrhagic shock as evidenced by Bar-Or et al. (US 2005/0215468) in paragraph [0004] where it describes ischemia occurs in hemorrhagic shock in a more generalized sense. Thus Pinsky meets claims 1-3, 10 and 11 because treating ischemia that occurs in hemorrhagic shock inherently treats the condition of hemorrhagic shock.

The Office Action at page 9, *sic* throughout. As the rejections and the disclosures of Fujita and Pinsky are similar, and the rejections are based on the same errors of fact and law, the rejections will be discussed together.

Neither Fujita nor Pinsky discloses expressly the use of CO in treatment of hemorrhagic shock. Nevertheless, the Office cites Bar-Or, apparently to support the proposition that ischemia and hemorrhagic shock are one and the same condition. This is a clear error of fact. The instant specification defines hemorrhagic shock as "shock brought on by a loss (e.g., an acute or chronic loss) of circulating blood volume and/or oxygen carrying capacity." Specification at paragraph [0037]. See also, *Webster's Medical Desk Dictionary* (1986), "shock"; Martel, 2002, "Hemorrhagic Shock," J. Obstet. Gynaecol. Can., 24:504-511, all previously of record. Ischemia, on the other hand, is defined as "localized tissue anemia due to obstruction of the inflow of arterial blood." *Webster's Medical Desk Dictionary* (1986), "ischemia", also previously of record. See also, Declaration of Dr. Brian S. Zuckerbraun, M.D., a surgeon at the University of Pittsburgh and inventor in the present application filed under 37 CFR § 1.132 on January 12, 2009 ("the Declaration"), discussed in further detail below. Ischemia and ischemic disorders can occur in the absence of blood loss and hemorrhagic shock, e.g., in such conditions as peripheral vascular disorder (obstruction of arteries in the arms and legs), venous thrombosis (a blood clot in a vein), pulmonary embolus (blockage of an artery in the lungs), myocardial infarction (blockage of a coronary artery), and sickle cell anemia (blockage of capillaries by abnormal red blood cells). See Pinsky at paragraph [0053]. Therefore, one of ordinary skill would recognize that the terms "ischemia" and "hemorrhagic shock" refer to distinct conditions and are not simply interchangeable. The fact that ischemia can be one potential aspect of hemorrhagic shock does not mean that hemorrhagic shock and ischemia are one and the

same thing. Ischemia can certainly occur in the absence of hemorrhagic shock. Applicants therefore submit that "ischemia" and "hemorrhagic shock" are not one and the same condition and that the terms cannot properly and fairly be construed by the Office as interchangeable.

Further, the Office has deemed that treatment of hemorrhagic shock is inherent in the disclosure of Fujita or Pinsky. It settled that to establish inherency, the missing element must necessarily be present in the reference and would be recognized by persons of ordinary skill.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) . . . ; In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). . . . "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) . . . .

MPEP § 2112 IV (emphasis added). The animals in the experiments described in Fujita and Pinsky were treated for ischemia of individual organs. Neither Fujita nor Pinsky recites or suggests that the animals were experiencing hemorrhagic shock, and treatment of hemorrhagic shock is not necessarily present in the disclosure of Fujita or Pinsky. For example, although Fujita shows that CO improved survival of mice who had been subjected to experimentally induced lung ischemia, there is absolutely no indication in Fujita that the mice experienced hemorrhagic shock. The mice were not subjected to a reduction of circulating or total blood volume. Rather, the left hilum of the lung, including the pulmonary artery, was clamped for a period of 1-1.5 hours to create an anemic condition in the lung tissue. There is no indication, or even suggestion, that the mice tested in Fujita necessarily experienced a significant reduction in circulating or total blood volume. Similarly, the examples provided by Pinsky involve only localized ischemia, with no indication that the animals necessarily suffered a significant reduction of circulating or total blood volume as observed in hemorrhagic shock. In Example 7, Pinsky discloses that CO was protective in a cerebral ischemia model of stroke. In Example 11, Pinsky discloses that CO was protective against ischemic damage in a model of lung transplantation. The disclosures do not indicate to skilled practitioners that the animals

necessarily experienced hemorrhagic shock. Rather, skilled practitioners would recognize that hemorrhagic shock was not present. Applicants respectfully submit that this is a clear error of fact.

Additionally, the Office has not even alleged that hemorrhagic shock was necessarily present in the mice treated with CO, as would be required in any attempt to establish a *prima facie* case of inherent anticipation. Rather, the Office argues that hemorrhagic shock is merely “not rule[d] out” by the disclosures of Fujita and Pinsky. The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency. The Office must provide a basis in fact and/or technical reasoning to reasonably support a determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. An allegation that hemorrhagic shock may have occurred is not sufficient. Applicants respectfully submit that this is a clear error of law.

Further, applicants submit that in an error of law, the Office refused to consider the Declaration of Dr. Brian Zuckerbraun in its finding of anticipation. The Office alleged that Bar-Or teaches that ischemia and hemorrhagic shock are equivalent. In reply, applicants submitted the Declaration to provide the Office with evidence regarding how a skilled practitioner, in this instance a physician, would have interpreted the terms. The Office refused to consider the Declaration, stating: “Declaration can not be used to overcome rejections under 35 USC 102.” Office Action page 14. However, where, as here, the Office relies on extraneous evidence in finding anticipation, other evidence that tends to contradict the Office’s position is clearly relevant and should be considered by the Office. See MPEP 2112 V. Failing to consider the Declaration is clear legal error.

Based on the clear errors of law and fact discussed above, applicants request review and withdrawal of the rejection of claims 1-3, 10, and 11 as inherently anticipated by either Fujita or Pinsky.

## II. The Office Has Not Established a *Prima Facie* Case of Obviousness

Claims 1, 55, and 56 were rejected as allegedly obvious over Fujita or Pinsky; and claims 1, 2, and 57-65 were rejected as allegedly obvious over Fujita or Pinsky in view of Peitzman. These rejections for alleged obviousness rely on the alleged inherent anticipation of claims 1 and 2 over Fujita or Pinsky. See the Office Action at pages 11 (“Fujita and Pinsky have been shown above individually to anticipate claim 1”) and 12 (“Fujita and Pinsky have been shown above individually to anticipate claims 1 and 2”). As discussed above, applicants respectfully submit that the rejection of claims 1 and 2 as allegedly anticipated by Fujita or Pinsky is based on clear errors of fact and law

and should be withdrawn. Absent a showing that the references disclose all limitations of claims 1 and 2, there is not a clear articulation of the reasons why the Office believes that the claims would have been obvious. Therefore, a *prima facie* case of obviousness has not been made, and applicants request review and withdrawal of the rejections for alleged obviousness.

### III. Conclusion

The Office's rejection of claims 1-3, 10, and 11 for alleged inherent anticipation over Fujita or Pinsky is based on clear errors of fact and/or law. The Office has not demonstrated or alleged that any of the references inherently disclose all of the limitations of any of the claims, and therefore has failed to establish a *prima facie* case of anticipation. Applicants request withdrawal of the rejections for alleged anticipation.

Additionally, the rejections of claims 1, 55, and 56 as allegedly obvious over Fujita or Pinsky and claims 1, 2, and 57-65 as allegedly obvious over Fujita or Pinsky in view of Peitzman are based on the clearly erroneous rejection of claims 1 and 2 for alleged inherent anticipation. Applicants request withdrawal of the rejections for alleged obviousness.

Applicants do not concede any positions of the Office that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

This Request is being submitted with a Notice of Appeal and the required fee. Please apply any required charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14022-0011001.

Respectfully submitted,

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